**Supplemental Information for *"Meta-analysis of cannabinoid ligand binding affinity and cannabinoid receptor distribution: interspecies differences,"* by McPartland, Glass, Pertwee**

**Supplementary Table S-7 and Table S-8 and Table S-9**

**Table S-7**
**Sensitivity analysis One: affinity data from Table 2 and Table 3 transformed into rank orders, compared to affinity rank orders derived from bubble-sort of data in Supplemental Table S-6.[1]**

| receptor | data source | aggregate rank order of ligand affinity |
|---|---|---|
| *Hs*$CB_1$ | from Tables 2 and 3 | HU>CP≈SR>WIN>THC>AEA>CBN>2AG |
| | bubble-sort rank order | HU>CP>SR>WIN≈THC>AEA>CBN>2AG (n=31) |
| *Rn*$CB_1$ | from Tables 2 and 3 | HU>CP≈SR>WIN»THC>AEA>CBN>2AG>CBD |
| | bubble-sort rank order | HU>CP≈SR>WIN>THC>AEA>CBN>2AG>CBD (n=38) |
| *Hs*$CB_2$ | from Tables 2 and 3 | HU>CP>WIN>THC>CBN>AEA>2AG>CBD |
| | bubble-sort rank order | HU>CP≈WIN»THC>CBN>AEA>2AG>CBD (n=29) |
| *Rn*$CB_2$ | from Tables 2 and 3 | CP>THC>AEA>CBD>2AG |
| | bubble-sort rank order | CP>WIN>THC≈AEA>2AG (n=12) |

[1] rank order of ligands based on scalar transformation of affinity values (nM units), where (≈) = affinity values within a factor of 1.5 from each other; (>) = affinity values between 1.5- and 10-fold from each other; (») = affinity values greater than 10-fold from each other.
n = number of aggregated studies from Supplemental Table S-6.

**Table S-8**
**Sensitivity analysis Two: meta-analytic affinity ratios (calculated from Table 2 and Table 3) compared to affinity ratios measured in direct *in vitro* comparisons[1]**

| ligand | *Hs*CB$_1$ : *Rn*CB$_1$ | *Hs*CB$_2$ : *Rn*CB$_2$ | *Hs*CB$_1$ : *Hs*CB$_2$ | *Rn*CB$_1$ : *Rn*CB$_2$ |
|---|---|---|---|---|
| | **0.59** | **2.7** | **0.71** | **3.3** |
| THC | 0.25 (*3*) 0.15 - 0.4 | 0.5 (*1*) | 0.75 (*8*) 0.1 - 1.6 | 5.5 (*2*) 2.0 - 9.1 |
| | nc | **2.9** | **nc** | **2.2** |
| CBD | nc | nc | nc | nc |
| | **1.43** | **nc** | **3.1** | **nc** |
| CBN | nc | nc | 2.8 (*3*) 1.2 - 3.8 | nc |
| | **2.7** | **1.64** | **0.54** | **0.33** |
| AEA | 1.5 (*1*) | 1.0 (*3*) 0.1 - 2.3 | 0.82 (*7*) 0.2 - 2.4 | 0.32 (*3*) 0.30 - 0.36 |
| | **2.9** | **0.63** | **2.87** | **0.62** |
| 2-AG | nc | 0.3 (*1*) | 0.31 (1) | nc |
| | **0.73** | **nc** | **0.63** | **nc** |
| HU210 | 0.83 (*2*) 0.6 - 1.1 | nc | 1.26 (*5*) 0.01 - 2.9 | nc |
| | **2.55** | **1.1** | **2.7** | **1.67** |
| CP55,940 | 1.6 (*7*) 0.4 - 3.4 | 1.5 (*5*) 0.3 - 2.9 | 1.9 (*19*) 0.42 - 8.7 | 1.3 (*7*) 0.2 - 4.0 |
| | **7.0** | **nc** | **4.5** | **nc** |
| WIN55212-2 | 24.1 (*3*) 0.45 - 70.5 | 2.0 (*4*) 0.2 - 6.7 | 16.4 (*10*) 1.3 - 28.5 | 1.5 (*3*) 0.1 - 3.7 |
| | **2.9** | **nc** | **nc** | **nc** |
| SR141716A | 2.6 (*3*) 0.63 - 4.5 | 1.15 (*3*) 1.0 - 1.3 | 0.012 (*8*) 0,001 - 0.02 | 0.0007 (*3*) 0.0 - 0.002 |

[1]Each cell in the Table contains two lines of data:
**Line 1:** Affinity ratios calculated from Table 2 and Table 3 in red-colored font. Example: THC ratio *Hs*CB$_1$ / *Rn*CB$_1$ = 25.1 nM / 42.6 nM = 0.59.
**Line 2**: Affinity ratios measured in direct *in vitro* comparisons reported in the literature (from column 7 of Supplemental Table S-1): mean affinity ratios, followed by number of comparative studies (*n* in parentheses), followed by the range reported in the literature. Note that Line 2 included Kd *and* Ki ratios for CP55,940, WIN55212-2, and SR141716A, whereas Line 1 included only Kd data (which was lacking for WIN55212-2 and SR141716A at *Rn*CB2 and *Hs*CB2); nc = no comparisons in literature.

**Table S-9**
**Sensitivity analysis Three: ligand affinity at *Rn*$CB_1$ and *Rn*$CB_2$ (from Table 2 and Table 3) compared to ligand affinity at *Mm*$CB_1$ and *Mm*$CB_2$ (from Supplemental Table S-2)**[1]

| ligand | *Rn*$CB_1$ vs. *Mm*$CB_1$ | *Rn*$CB_2$ vs. *Mm*$CB_2$ |
|---|---|---|
| THC | ***Rn:* 42.6 ±5.01, *18***<br>*Mm*: 76.6 ±30.2, *5*<br>no difference, $p = 0.069$ | ***Rn:* 13.0 ±7.70, *3***<br>*Mm*: 13.4 ±5.3, *4*<br>no difference, $p = 0.970$ |
| CBD | ***Rn:* 2210.5 ±558.08, *6***<br>*Mm*: 4900, *1*<br>nc | ***Rn:* 1000, *1***<br>*Mm*: nd<br>nc |
| CBN | ***Rn:* 368.0 ±121.14, *8***<br>*Mm*: nd<br>nc | ***Rn:* nd**<br>*Mm*: 2.3, *1*<br>nc |
| AEA | ***Rn:* 87.7 ±11.32, *26***<br>*Mm*: 746.9 ±291.6, 8<br>different, $p = 0.001$ | ***Rn:* 267.8 ±67.94, *5***<br>*Mm*: 1399.0 ±394.1, 4<br>different, $p = 0.015$ |
| 2-AG | ***Rn:* 1180.5 ±538.59, *4***<br>*Mm*: 1626.6 ±600.6, *3*<br>no difference, $p = 0.606$ | ***Rn:* 1900.0 ±1800.0, *2***<br>*Mm*: 94, *1*<br>nc |
| HU210 | ***Rn:* 0.34 ±0.102, *7***<br>*Mm*: 1.56, *1*<br>nc | ***Rn:* nd**<br>*Mm*: nd<br>nc |
| [$^3$H]CP55,940 | ***Rn:* 0.98 ±0.12, *51***<br>*Mm*: 1.7 ±0.34, *12*<br>different, $p = 0.016$ | ***Rn:* 0.84 ±0.304, *8***<br>*Mm*: 0.51 ±0.14, *4*<br>no difference, $p = 0.483$ |
| [$^3$H]WIN55212-2 | ***Rn:* 2.4 ±0.348, *13***<br>*Mm*: 1.9 ±0.32, *4*<br>no difference, $p = 0.464$ | ***Rn:* nd**<br>*Mm*: nd<br>nc |
| [$^3$H]SR141716A | ***Rn:* 1.0 ±0.22, *19***<br>*Mm*: 0.25 ±0.08, *7*<br>different, $p = 0.047$ | ***Rn:* nd**<br>*Mm*: nd<br>nc |

[1]Each cell in the Table contains three lines of data:
**Line 1:** *Rn*CB1 and *Rn*CB2 data from from Table 2 and Table 3, reported as means (nM) ± standard error, and *number* of studies.
**Line 2:** *Mm*CB1 and *Mm*CB2 data reported as means (nM) ± standard error, and *number* of studies; extracted from Supplemental Table S-2; Ki for THC, CBD, CBN, AEA, 2-AG, and HU210; Kd of CP55,940, WIN55212-2, and SR141716A; nd = no data; nc = insufficient data to calculate
**Line 3:** Statistical difference between *Rn* and *Mm* means (SYSTAT, Evanston, IL), nc = not calculated